The trithorax group proteins Kismet and ASH1 promote H3K36 dimethylation to counteract Polycomb group repression in Drosophila.

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Public Summary:
Members of the Polycomb group of repressors and trithorax group of activators maintain heritable states of transcription by modifying nucleosomal histones or remodeling chromatin. Although tremendous progress has been made toward defining the biochemical activities of Polycomb and trithorax group proteins, much remains to be learned about how they interact with each other and the general transcription machinery to maintain on or off states of gene expression. The trithorax group protein Kismet (KIS) is related to the SWI/SNF and CHD families of chromatin remodeling factors. KIS promotes transcription elongation, facilitates the binding of the trithorax group histone methyltransferases ASH1 and TRX to active genes, and counteracts repressive methylation of histone H3 on lysine 27 (H3K27) by Polycomb group proteins. Here, we sought to clarify the mechanism of action of KIS and how it interacts with ASH1 to antagonize H3K27 methylation in Drosophila. We present evidence that KIS promotes transcription elongation and counteracts Polycomb group repression via distinct mechanisms. A chemical inhibitor of transcription elongation, DRB, had no effect on ASH1 recruitment or H3K27 methylation. Conversely, loss of ASH1 function had no effect on transcription elongation. Mutations in kis cause a global reduction in the di- and tri-methylation of histone H3 on lysine 36 (H3K36) Eth modifications that antagonize H3K27 methylation in vitro. Furthermore, loss of ASH1 significantly decreases H3K36 dimethylation, providing further evidence that ASH1 is an H3K36 dimethylase in vivo. These and other findings suggest that KIS antagonizes Polycomb group repression by facilitating ASH1-dependent H3K36 dimethylation.

Scientific Abstract:
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